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REMARKS/ARGUMENTS

Claims 2, 4, and 10-13 have been cancelled. Claims 1, 3, 5-6, 8 and 14-20 are pending.

Applicants are filing herewith a Request for Continued Examination (RCE) due to the finality of the Office Action, and the appropriate fee.

Claims 1, 5, 6 and 8 have been amended. No new matter has been added by virtue of these amendments and their entry is respectfully requested.

Claim Objections

Claim 1 is objected to because of grammatical informalities. The term "a" has been replaced by "an" in claim 1.

Claim 1 is objected to for the limitation "and the second subculture with the second test substance" has been replaced with the phrase "a second test substance" as per the Examiner's recommendation.

Claim 1 is objected to for the recitation of "culturing the first and second subcultures between 7 to 18 days." Applicants have amended the claim to recite the phrase "culturing the first and second subcultures for 7 to 18 days" as per the Examiner's recommendation.

Claim Rejections Under 35 U.S.C. §112

Claim 1 was rejected under 35 U.S.C. § 112, second paragraph. The Examiner asserts on page 3 of the Office Action:

Claim 1 recites "a method for identifying a drug candidate for promoting tissue-specific differentiation of an embryonic stem cell" which comprises exposing two subcultures to distinct test substances, then exposing each subculture to two more differentiation test substances. As such, it appears that the test substances initially exposed are no longer the differentiation test substance, as there exist two more test substances which

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are named "differentiation test substance", and further, at best, the method identifies two, if not three, substances that induce differentiation. Hence, there appears to be an absence of a nexus between the claimed method in the preamble, and a step of identifying a test substance that promotes differentiation.

Claim 1 also recites the limitation "undifferentiated embryonic stem cells". As embryonic stem cells are necessarily not differentiated, otherwise they would be called the cell type which it has differentiated into, the metes and bounds of such limitation are unclear.

Claims 3 and 5-6 recites the limitations "the embryonic stem cells", "the murine embryonic stem cells", and "the mammalian embryonic stem cells", respectively, in claim 1. There is insufficient antecedent basis for this limitation in the claim. Specifically, it is noted that the cells of claim 1 are undifferentiated embryonic stem cells, and not limited to mammalian or murine either.

Claim 8 recites the "the conditions that would promote tissue-specific differentiation of stem cells" in claim 1. However, there is insufficient antecedent basis for this in claim 1. Moreover, it is unclear whether and when the subcultures are cultured in the conditions are before, during or after exposure to the various test substances, hence, the claim further lacks clarity for this aspect.

Claims 3, 5-6, 8, and 14-20 are also rejected for depending for depending rejected base claim(s) and not overcoming the lack of clarity in such base claim.

In response, Applicants have amended the claims. Claim 1 has been amended to remove the term "undifferentiated." Claims 3, 5-6 have been amended to provide the correct antecedent basis. Claim 8 has been amended to clarify that the test substances are added to each subculture which is incubated under appropriate conditions. Amendment and cancellation of the claims are not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were done solely to expedite prosecution and allowance of the application. Applicants reserve the right to pursue the claims as originally filed, or substantially similar claims, in this or one or more continuation patent applications.

No new matter has been added by virtue of these amendments and their entry is respectfully requested. In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

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Claim Rejections Under 35 U.S.C. § 112 New matter.

Claims 1, 3, 5-6, 8 and 14-20 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement.

In response Applicants have amended the claims to recite "at least about 5 days" and to clarify the addition of test substances. Amendment and cancellation of the claims are not to be construed as an acquiescence to any of the rejections/objections set forth in the instant Office Action, and were done solely to expedite prosecution and allowance of the application. Applicants reserve the right to pursue the claims as originally filed, or substantially similar claims, in this or one or more continuation patent applications.

No new matter has been added by virtue of these amendments and their entry is respectfully requested. In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

Claim Rejections Under 35 U.S.C. § 112, first paragraph.

Claims 1, 3, 5-6, 8 and 14-20 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement.

The Examiner asserts:

Applicant's claims are drawn to identifying a compound, but the complicated protocol uses at least four distinct compounds in various combinations, to identify differentiation compounds, hence, at best, it could only produce a pool of compounds, of which one is a potential compound for differentiation.

In response, Applicants have amended the claims. Applicants believe that this amendment overcomes the Examiner's rejections.

The Examiner further asserts:

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Next, Applicant's claims are drawn to using any undifferentiated ES cells, yet clearly mouse EB cells are used in the methods (p. 16). Moreover, the claims are drawn to any differentiation, yet, the disclosure is the induction of hepatocyte differentiation in such mouse EB cells, and no other differentiation pathway is disclosed to be produced in the method. However, the Art generally recognizes that such differentiation is specific to the type of ES cell, or any cell for that matter, due to the complexities of the pathways, which may differ between species as well as within any pathway. Hence, the conditions and timings of adding the different factors would necessarily differ. While this may not matter for something as simple as a single stage of differentiation, Applicant's claims encompass many stages, and due to the forgoing differences in conditions required, any specific cell type could not be possible, or may form the differentiated cell type before any candidate drugs are even added. For example, U.S. Patent No. 6,485,589 to Rambhatla discloses specific conditions where the cells automatically differentiate into hepatocytes by the addition of a single compound (EXAMPLE 1). Hence, the other additions would not be able to go through the other stages of differentiation, as they would have developed into hepatocytes on day 1. In addition, Ramblata uses human EB cells. Hence, for any particular type of cell and conditions, such differentiations may not take place through various stages, but may occur in a single stage and even before the addition of the compounds, as the growth conditions are distinct for any particular ES cell. Hence, using Applicant's method would not produce its desired result under optimal conditions, and further would require extensive experimentation to determine the set of conditions for any specific ES cell.

Therefore, it would be undue experimentation to find the conditions required for specific combinations of compounds required to produce, in the time frames given, hepatocytes or any other specific cell types.

Applicants submit that the invention is directed to whether a test substance causes differentiation of a stem cell and not whether a particular test substance induces differentiation to a specific cell type. That is if a test substance induces differentiation then that test substance can be examined further. Applicants can also identify which cell type it would differentiate into by identifying genes that are expressed. See, for example, page 10 lines 4-30 through to page 12, lines 1- 14. Furthermore, the test indicates whether a factor induces any changes in a stem cell. Applicants need only compare the differences of the undifferentiated stem cell with one exposed to a test substance.

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In view thereof, Applicants respectfully request reconsideration and withdrawal of the instant rejection.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks and reconsideration and withdrawal of all rejections. It is respectfully submitted that this application with claims 1, 3, 5, 6 8 and 14-20 is in condition for allowance. If there are any remaining issues or the Examiner believes that a telephone conversation with the Applicants' attorney would be helpful in expediting prosecution of this application, the Examiner is invited to call the undersigned at telephone number shown below.

This response is accompanied by a petition for a two month retroactive extension of time and the required fee. Although, Applicants believe that no further extensions of time are required with submission of this paper, Applicants request that this submission also be considered as a petition for any further extension of time if necessary. The Commissioner for Patents and Trademarks is hereby authorized to charge the amount due for any retroactive extensions of time and any deficiency in any fees due with the filing of this paper or credit any overpayment in any fees paid on the filing or during prosecution of this application to Deposit Account No. 50-0951.

Respectfully submitted,
AKERMAN SENTERFITT

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